IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of: Gill	Group Art Unit: 3763
Serial No. 10/505,240	Examiner: DESANTO, Matthew F.
Filed: 02/22/05	Confirmation No.: 7416

For: CATHETER AND GUIDE TUBE FOR INTRACEREBRAL APPLICATION

Attorney Docket No: 0252.00003

DECLARATION

I, Steven Streatfield Gill, being duly sworn, do hereby state that:

1. I am the inventor of the above-captioned application.

2. I am skilled in the art and have worked extensively in the field of neurosurgery and neurosurgical catheters.

3. Claims 1-25 stand rejected under 35 U.S.C. §103(a) as being unpatentable over Gill and further in view of Eggers, et al. and U.S. Patent No. 6,719,727 to Brimhall, et al.

Neither Gill nor Eggers, et al. disclose each and every limitation of the presently pending claims, i.e. the catheter diameter being 1 mm or less and the stop surface and hub structure.

More specifically, Gill (an earlier patent by myself) discloses placing a 1 mm diameter electrode in the subthalamic nucleus is technically demanding in column 7, but does not disclose any diameter with respect to the guide tube itself. Furthermore, Gill teaches away from a diameter of a guide wire less than 1 mm because it is likely to be deflected from its target by resistance in the tissues and that a larger diameter guide wire is preferred (column 7, lines 36-49). Gill does not disclose a catheter with a fine tube having an external diameter of 1 mm or less. Furthermore, Gill does not disclose a catheter having a stop surface or hub as required in the presently pending claims.

Eggers, et al. includes a fluid path for dispensing a conductive fluid to the region of the brain to be ablated in addition to the electrodes, shown in detail in Figure 2. In other words, Eggers, et al. discloses multiple tubes, whereas the present invention is directed to a single fine tube. The present invention does not

include multiple fluid tubes and an electrode as described in Eggers, et al., and any fluid that might be delivered is delivered itself through the single fine tube. Claim 1 has been amended to reflect this point. Furthermore, Eggers, et al. does not disclose a catheter with any kind of stop or a hub. The stop surface of the hub is important in order to set the depth of insertion of the fine tube in the brain parenchyma. Without the hub and stop surface, there is a risk that the fine tube would be inserted too far and damage brain tissue.

Brimhall, et al. discloses an intravascular catheter assembly that has a catheter adapter 24 which links a first tube 21 for insertion into a vein with a larger diameter tube 25 for connection to a fluid supply (e.g. a drip). Intravascular catheter assemblies of this type have been widely used for many years. While the Brimhall, et al. device may look similar upon first glance to the catheter of the present invention, they are quite different. Brimhall, et al. does not make up for the deficiencies of Gill and Eggers, et al. Furthermore, one skilled in the art would not look to Brimhall, et al. in order to modify Gill and Eggers, et al. because an intravascular catheter is not considered suitable for use in neurosurgery.

Brimhall, et al. does not disclose a tube of less than 1 mm in diameter and only discloses intravascular catheters (i.e. not catheters for insertion into the brain parenchyma). Thus, the Brimhall, et al. device is designed and used for a completely different purpose than the neurosurgical catheter of the present invention. During insertion into a vein, the catheter tube 21 of the Brimhall, et al. device is stiffened by a needle. The needle and tube together penetrate the skin allowing the tube to be inserted into the selected vein. The direction of insertion into the body is controlled manually by the clinician and with wings 26 provide the clinician with a better grip of the device thereby making insertion into the vein easier (see paragraphs 3 and 39-40 of Brimhall, et al.). The clinician would typically almost fully insert the catheter 21 into the vein, but would typically leave a small proximal length of the catheter 21 exposed before securing the wings to the patient's skin (i.e. using tape or sutures).

Brimhall, et al. further does not disclose a stop surface as in the present invention. While there is a step change in diameter between the tube 21 and catheter adapter 24, the device would not be used as a stop surface. In particular, the Brimhall device is inserted into the body at a shallow angle, and there is no reference surface against which the catheter 24 adapter could abut. The catheter adapter of Brimhall, et al. therefore does not set the depth of catheter insertion into

the vein by acting as a stop surface; instead, the depth of insertion is manually controlled by the clinician.

Thus, neither Gill, Eggers, et al., or Brimhall, et al. disclose each and every limitation of the present invention.

Furthermore, the present invention provides unexpected results of precise targeting while delivering drugs and reduced brain trauma due to the size of the fine tube and the function of the stop surface.

The goal of a surgeon using a neurosurgical catheter is to minimize reflux or backflow of drug, avoid tearing tissue upon insertion of the catheter, and controlled perfusion of the drug at a specific target within the brain. Before the present invention, this was not possible. In any other catheter in the prior art that is used for drug delivery to the brain, the drug follows the path of least resistance upon exiting the tip of the catheter. In general, the drug permeates a broad area of tissue, i.e. a nonspecific area of tissue, which can cause damage to healthy brain tissue. Furthermore, prior art catheters have larger diameter tubes which cause tearing of brain tissue, adding additional damage.

See attached reference "Reflux-free cannula for convection-enhanced high-speed delivery of therapeutic agents" by Krauze, et al., J Neurosurg 103:923-929, 2005. This reference describes the problems of current cannulas with reflux and low flow rates due to large diameters. Different size diameters were analyzed in the experiments. Figure 1(a) shows the amount of reflux with each diameter of catheter. Larger diameters experienced more reflux. The results were that smaller diameters allowed for higher flow rates.

The present invention overcomes these problems in the art by using a fine tube with an external diameter of not more than 1.0 mm, and even smaller in some embodiments (0.7 mm, 0.5 mm). By using such a small tube, point delivery of a drug to specific brain tissue can be accomplished without tearing of tissue upon insertion. More importantly, deep brain tissue can be targeted with the present invention. By including the stop surface, the tip of the catheter is maintained at the correct position in order to delivery drug to only the desired target tissue. The stop also prevents over-penetration and the subsequent need for retraction of the catheter tip during the implantation procedure. In particular, it has been found that over-penetration of the catheter into brain tissue by only 1 mm causes a microcavity to form in the brain tissue. Pumping an infusate down the catheter then causes this cavity to expand, which degrades the infusate distribution profile within the brain

tissue thereby reducing treatment efficacy. Having the stop on the catheter prevents such over-penetration.

See paragraph [0036] in the specification:

As explained above, insertion of a catheter into particularly sensitive regions of the brain leads to trauma on insertion which surgeons wish to minimise. The finer the catheter the less trauma the brain experiences. However, since the accuracy of insertion is crucially important, and since these particularly sensitive areas of the brain are a considerable distance from the skull surface, larger diameter catheters have been considered to be necessary in order to accurately place the distal end of the catheter. However, the present invention allows much finer catheters to be used.

See also paragraph [0001]:

The present invention relates to apparatus for use in neurosurgery, and to a method of positioning neurosurgical apparatus. The apparatus and method are particularly useful in stereotactically targeting treatment of abnormalities of brain function, and for the infusion of therapeutic agents directly into the brain parenchyma. This would be particularly useful when a therapeutic agent given systemically will have widespread unwanted side effects which would be avoided by confining the delivery to the malfunctioning or damaged brain tissue.

Since neither the cited references alone or in combination with knowledge in the art suggest the currently claimed invention, it is consequently respectfully submitted that the claims are clearly patentable over the combination, even if the combination were to be applied in opposition to applicable law, and reconsideration of the rejection is respectfully requested.

The undersigned declares further all statements made herein of his knowledge are true and that all statements made upon information and belief are believed to be true, and further that the statements were made with the knowledge that willful and false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issuing thereon.

Date: 6th October, 2009

Steven Gill.

Steven Streatfield Gill